A mixture of 4-[2*S*-(3-Benzyloxycarbamoyl-2*R*-cyclopentylmethyl-propionylamino)-3,3-dimethyl-butyryl]-piperazine-1-carboxylic acid phenyl ester Intermediate 3 (172 mg, 0.283 mmol), cyclohexene (1 ml) and Palladium-on-carbon (10%, 52 mg) in ethanol (10 ml) was stirred under reflux for 1 hour. Filtration over celite and purification by prep. HPLC yielded the title comopund (67 mg, 46%) as colourless needles. LRMS: +ve ion 539 [$M+Na^+$, 100%],], -ve ion 561 [$M+HCO_2^-$, 100%], ^{1}H-NMR (250MHz), δ (MeOH-*d*4) 7.95 (1H, bd, J 8.9Hz, NH), 7.41-7.10 (5H, 3m, 5 ArH), 4.90 (1H, d, J 8.9Hz, *tert*-ButylCH), 4.18-3.47 (8H, m, 4 CH_2N-piperazine), 2.91 (1H, m, $CH_2\underline{CH}CH_2$), 2.34 (1H, dd, J_1 7.8, J_2 14.5Hz, 0.5 $COCH_2$), 2.20 (1H, dd, J_1 6.5, J_2 14.5Hz, 0.5 $COCH_2$), 1.83-1.27 (11H, 4 CH_2-cyclopentyl, CH-cyclopentyl, CH_2), 1.03 (9H, 2s, $C(CH_3)_3$)

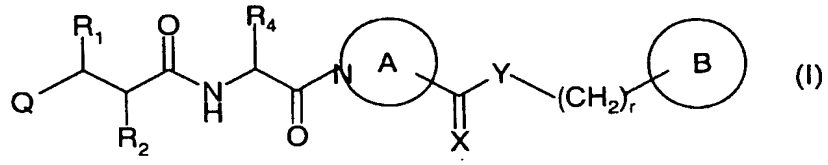
Biological Example

Minimal Inhibitory concentrations (MIC) of inhibitors against *Streptococcus pneumoniae* ATCC 49619 were determined by a standard agar plate dilution method following recommendations in **British Society for Antimicrobial Chemotherapy Working Party**. 1991. "A guide to sensitivity testing British Society for Antimicrobial Chemotherapy, London, United Kingdom". Briefly Iso-Sensitest agar (pH 7.2: Oxoid, United Kingdom) was employed supplemented with 5% horse blood (Oxoid) and 20 □g of NAD (Sigma) per ml to support growth of fastidious bacteria. The inoculum used was approximately 10^4 colony forming units of each isolate contained in a volume of 1 □l. Plates were incubated 18 to 24 hr in air, or for fastidious bacteria an atmosphere enriched with 4-6% carbon dioxide at 35°C. The MIC was determined as the lowest concentration of an antimicrobial tested that inhibited growth of the inoculum, disregarding a single persisting colony or faint haze caused by the inoculation.

By way of example, in the above test the compounds of Examples 3, 4 and 5 herein had MICs in the range <0.125 to 0.25 μg/ml.

Claims:

1. A compound of formula (II), or a pharmaceutically or veterinarily acceptable salt, hydrate or solvate thereof



(I)

wherein:

Q represents a radical of formula -N(OH)CH(=O) or formula -C(=O)NH(OH);

R_1 represents hydrogen, methyl or trifluoromethyl or, except when Q is a radical of formula -N(OH)CH(=O), a hydroxy, halo or amino group;

R_2 represents a group R_{10}-$(D)_n$-$(ALK)_m$- wherein

R_{10} represents hydrogen, or an optionally substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, aryl, or heterocyclyl group and

ALK represents a straight or branched divalent C_1-C_6 alkylene, C_2-C_6 alkenylene, or C_2-C_6 alkynylene radical, and may be interrupted by one or more non-adjacent -NH-, -O- or -S- linkages,

D represents -NH-, -O- or -S-, and

m and n are independently 0 or 1;

R_4 represents the side chain of a natural or non-natural alpha amino acid;

ring A represents an optionally substituted monocyclic heterocyclic ring containing from 5 to 7 ring atoms, one of which is the nitrogen atom shown, the remaining ring atoms being selected from compatible combinations of carbon, oxygen, sulfur and nitrogen;

X is oxygen or sulfur;

Y is oxygen, sulfur or -NH-;

R is 0, 1, 2 or 3; and

ring B represents an optionally substituted carbocyclic or heterocyclic ring system.

2. A compound as claimed in claim 1 wherein R is hydrogen.

3. A compound as claimed in claim 1 or claim 2 wherein R_2 is:

optionally substituted C_1-C_8 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl or cycloalkyl;

phenyl(C_1-C_6 alkyl)-, phenyl(C_3-C_6 alkenyl)- or phenyl(C_3-C_6 alkynyl)- optionally substituted in the phenyl ring;

cycloalkyl(C_1-C_6 alkyl)-, cycloalkyl(C_3-C_6 alkenyl)- or cycloalkyl(C_3-C_6 alkynyl)- optionally substituted in the cycloalkyl ring;

heterocyclyl(C_1-C_6 alkyl)-, heterocyclyl(C_3-C_6 alkenyl)- or heterocyclyl(C_3-C_6 alkynyl)- optionally substituted in the heterocyclyl ring; or

$CH_3(CH_2)_pO(CH_2)_q$- or $CH_3(CH_2)_pS(CH_2)_q$-, wherein p is 0, 1, 2 or 3 and q is 1, 2 or 3.

4. A compound as claimed in claim 1 or claim 2 wherein R_2 is methyl, ethyl, n- or iso-propyl, n- or iso-butyl, n-pentyl, iso-pentyl 3-methyl-but-1-yl, n-hexyl, n-heptyl, n-acetyl, n-octyl, methylsulfanylethyl, ethylsulfanylmethyl, 2-methoxyethyl, 2-ethoxyethyl, 2-ethoxymethyl, 3-

hydroxypropyl, allyl, 3-phenylprop-3-en-1-yl, prop-2-yn-1-yl, 3-phenylprop-2-yn-1-yl, 3-(2-chlorophenyl)prop-2-yn-1-yl, but-2-yn-1-yl, cyclopentyl, cyclohexyl, cyclopentylmethyl, cyclopentylethyl, cyclopentylpropyl, cyclohexylmethyl, cyclohexylethyl, cyclohexylpropyl, furan-2-ylmethyl, furan-3-methyl, tetrahydrofuran-2-ylmethyl, tetrahydrofuran-2-ylmethyl, piperidinylmethyl, phenylpropyl, 4-chlorophenylpropyl, 4-methylphenylpropyl, 4-methoxyphenylpropyl, benzyl, 4-chlorobenzyl, 4-methylbenzyl, or 4-methoxybenzyl.

5. A compound as claimed in claim 1 or claim 2 wherein R_2 is (C_1-C_6)alkyl-, cycloalkylmethyl-, (C_1-C_3)alkyl-S-(C_1-C_3)alkyl-, or (C_1-C_3)alkyl-O-(C_1-C_3)alkyl-, especially n-propyl, n-butyl, n-pentyl, cyclopentylmethyl, cyclopentylethyl, cyclohexylmethyl or cyclohexylethyl.

6. A compound as claimed in any of the preceding claims wherein R_4 is:

the characterising group of a natural α amino acid, for example benzyl, or 4-methoxyphenylmethyl, in which any functional group may be protected, any amino group may be acylated and any carboxyl group present may be amidated; or

a group -[Alk]$_n$$R_9$ where Alk is a (C_1-C_6)alkylene or (C_2-C_6)alkenylene group optionally interrupted by one or more -O-, or -S- atoms or -N(R_{12})- groups [where R_{12} is a hydrogen atom or a (C_1-C_6)alkyl group], n is 0 or 1, and R_9 is hydrogen or an optionally substituted phenyl, aryl, heterocyclyl, cycloalkyl or cycloalkenyl group or (only when n is 1) R_9 may additionally be hydroxy, mercapto, (C_1-C_6)alkylthio, amino, halo, trifluoromethyl, nitro, -COOH, -CONH$_2$, -COOR^A, -NHCOR^A, -CONHR^A, -NHR^A, -NR^{A}R^B, or -CONR^{A}R^B wherein R^A and R^B are independently a (C_1-C_6)alkyl group; or

a benzyl group substituted in the phenyl ring by a group of formula -OCH_2COR_8 where R_8 is hydroxyl, amino, (C_1-C_6)alkoxy, phenyl(C_1-

C_6)alkoxy, (C_1-C_6)alkylamino, di((C_1-C_6)alkyl)amino, phenyl(C_1-C_6)alkylamino; or

a heterocyclic(C_1-C_6)alkyl group, either being unsubstituted or mono- or di-substituted in the heterocyclic ring with halo, nitro, carboxy, (C_1-C_6)alkoxy, cyano, (C_1-C_6)alkanoyl, trifluoromethyl (C_1-C_6)alkyl, hydroxy, formyl, amino, (C_1-C_6)alkylamino, di-(C_1-C_6)alkylamino, mercapto, (C_1-C_6)alkylthio, hydroxy(C_1-C_6)alkyl, mercapto(C_1-C_6)alkyl or (C_1-C_6)alkylphenylmethyl; or

a group $-CR_aR_bR_c$ in which:

each of R_a, R_b and R_c is independently hydrogen, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, phenyl(C_1-C_6)alkyl, (C_3-C_8)cycloalkyl; or

R_c is hydrogen and R_a and R_b are independently phenyl or heteroaryl such as pyridyl; or

R_c is hydrogen, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, phenyl(C_1-C_6)alkyl, or (C_3-C_8)cycloalkyl, and R_a and R_b together with the carbon atom to which they are attached form a 3 to 8 membered cycloalkyl or a 5- to 6-membered heterocyclic ring; or

R_a, R_b and R_c together with the carbon atom to which they are attached form a tricyclic ring (for example adamantyl); or

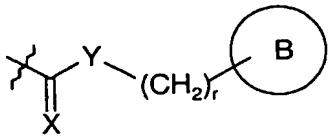
R_a and R_b are each independently (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, phenyl(C_1-C_6)alkyl, or a group as defined for R_c below other than hydrogen, or R_a and R_b together with the carbon atom to which they are attached form a cycloalkyl or heterocyclic ring, and R_c is hydrogen, -OH, -SH, halogen, -CN, -CO_2H, (C_1-C_4)perfluoroalkyl, -CH_2OH, -CO_2(C_1-C_6)alkyl, -O(C_1-C_6)alkyl, -O(C_2-C_6)alkenyl, -S(C_1-C_6)alkyl, -SO(C_1-C_6)alkyl, -SO_2(C_1-C_6) alkyl, -S(C_2-C_6)alkenyl, -SO(C_2-C_6)alkenyl, -SO_2(C_2-

C_6)alkenyl or a group -Q-W wherein Q represents a bond or -O-, -S-, -SO- or -SO_2- and W represents a phenyl, phenylalkyl, (C_3-C_8)cycloalkyl, (C_3-C_8)cycloalkylalkyl, (C_4-C_8)cycloalkenyl, (C_4-C_8)cycloalkenylalkyl, heteroaryl or heteroarylalkyl group, which group W may optionally be substituted by one or more substituents independently selected from, hydroxyl, halogen, -CN, -CO_2H, -CO_2(C_1-C_6)alkyl, -$CONH_2$, -CONH(C_1-C_6)alkyl, -CONH(C_1-C_6alkyl)$_2$, -CHO, -CH_2OH, (C_1-C_4)perfluoroalkyl, -O(C_1-C_6)alkyl, -S(C_1-C_6)alkyl, -SO(C_1-C_6)alkyl, -SO_2(C_1-C_6)alkyl, -NO_2, -NH_2, -NH(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, -NHCO(C_1-C_6)alkyl, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_8)cycloalkyl, (C_4-C_8)cycloalkenyl, phenyl or benzyl.

7. A compound as claimed in any of claims 1 to 5 wherein R_4 is methyl, ethyl, benzyl, 4-chlorobenzyl, 4-hydroxybenzyl, phenyl, cyclohexyl, cyclohexylmethyl, pyridin-3-ylmethyl, tert-butoxymethyl, naphthylmethyl, iso-butyl, sec-butyl, tert-butyl, 1-benzylthio-1-methylethyl, 1-methylthio-1-methylethyl, 1-mercapto-1-methylethyl, 1-methoxy-1-methylethyl, 1-hydroxy-1-methylethyl, 1-fluoro-1-methylethyl, hydroxymethyl, 2-hydroxethyl, 2-carboxyethyl, 2-methylcarbamoylethyl, 2-carbamoylethyl, or 4-aminobutyl.

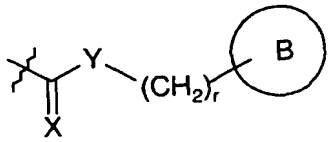
8. A compound as claimed in any of claims 1 to 5 wherein R_4 is tert-butyl, iso-butyl, benzyl, isopropyl or methyl.

9. A compound as claimed in any of the preceding claims wherein ring A is optionally substituted 1-pyrrolidinyl, piperidin-1-yl, 1-piperazinyl, hexahydro-1-pyridazinyl, morpholin-4-yl, tetrahydro-1,4-thiazin-4-yl, tetrahydro-1,4-thiazin-4-yl 1-oxide, tetrahydro-1,4-thiazin-4-yl 1,1-dioxide, hexahydroazipino, thiomorpholino, diazepino, thiazolidinyl or octahydroazocino.



10. A compound as claimed in any of claims 1 to 8 wherein ring A is piperidin-1-yl or 1-piperazin-4-yl.

11. A compound as claimed in any of the preceding claims wherein the grouping

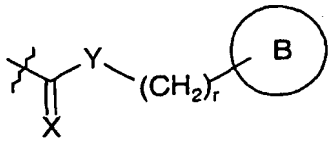


present in compounds (I) is attached to a ring carbon atom or a second ring nitrogen atom of ring A.

12. A compound as claimed in any of the preceding claims wherein r is 0 or 1.

13. A compound as claimed in any of the preceding claims wherein ring B is optionally substituted phenyl, 2-, 3- or 4-pyridyl, 9H-fluoren-9-yl, naphthyl, or 4-benzo[1,3]dioxol-5-yl.

14. A compound as claimed in any of the preceding claims wherein in the grouping



present in compounds (I), X is oxygen or sulphur when Y is -NH-, or both X and Y are oxygen.

15. A compound as claimed in claim 1 which is specifically named and characterised herein.

16. The use of a compound as claimed in any of the preceding claims in the preparation of an antimicrobial composition.